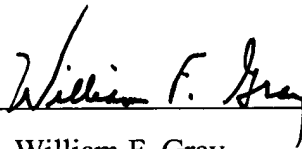


The amendment to structure (A1) in claim 1 is to clarify the drawing. Swiss-type use claims 1-8 have been converted into method of treatment claims. Claims 9-11 now refer to pharmaceutical compositions rather than medicaments. Claim 12 now refers to a process for preparing the pharmaceutical composition.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version with markings to show changes made.**"

In view of the above amendments and explanations, this application is deemed to be in condition for allowance, and allowance is accordingly requested.

Respectfully submitted,



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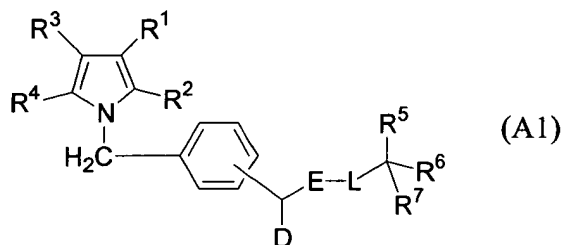
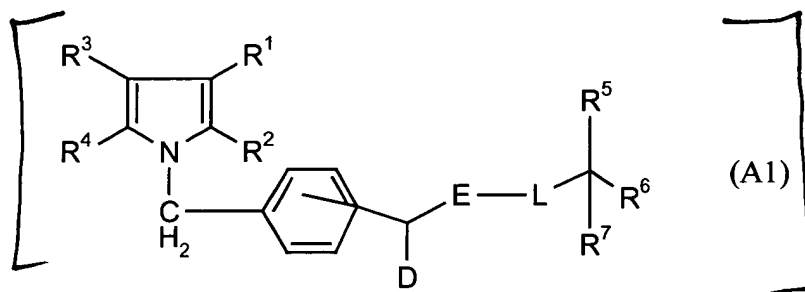
Date: 20 Dec '01

Version with markings to show changes made:

In the claims:

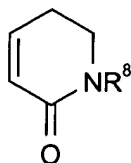
Claims 1-12 have been amended as shown below:

- (Amended) [Use of] A method for the prophylaxis or treatment of cardiovascular diseases which comprises administering an effective amount of a combination of component A and component B, component A being at least one MTP inhibitor [as component A] of the general formula (A1)



in which

R¹ and R², including the double bond connecting them, together form a phenyl or pyridyl ring or a ring of the formula



in which

R⁸ denotes hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

R³ and R⁴, including the double bond connecting them, together form a phenyl ring or a 4- to 8-membered cycloalkene or oxocycloalkene radical,

all ring systems mentioned under R¹/R² and R³/R⁴ optionally being substituted up to 3 times, identically or differently, by halogen, trifluoromethyl, carboxyl, hydroxyl, by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

D represents hydrogen, cycloalkyl having 4 to 12 carbon atoms or straight-chain or branched alkyl having up to 12 carbon atoms,

E represents the -CO- or -CS- group,

L represents an oxygen or sulphur atom or a group of the formula -NR⁹,

in which

R⁹ denotes hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl or phenyl,

R⁵ denotes phenyl or a 5- to 7-membered saturated or unsaturated heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O,

the cyclic systems optionally being substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

and/or the cyclic systems optionally being substituted by a group of the formula $-OR^{10}$ or $-NR^{11}R^{12}$,

in which

R^{10} denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

R^{11} and R^{12} are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms or straight-chain or branched acyl having up to 8 carbon atoms, which is optionally substituted by a group of the formula $-NR^{13}R^{14}$,

in which

R^{13} and R^{14} are identical or different and denote hydrogen or straight-chain or branched acyl having up to 8 carbon atoms,

R^6 represents hydrogen, carboxyl or straight-chain or branched alkoxycarbonyl having up to 5 carbon atoms,

or represents straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl or by a group of the formula -O-CO-R¹⁵,

in which

R¹⁵ denotes phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl or by straight-chain or branched alkyl having up to 5 carbon atoms,
or denotes straight-chain or branched alkyl or alkenyl each having up to 22 carbon atoms, each of which is optionally substituted by a group of the formula -OR¹⁶,

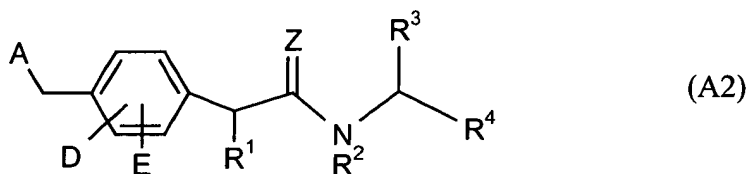
in which

R¹⁶ denotes hydrogen, benzyl, triphenylmethyl or straight-chain or branched acyl having up to 6 carbon atoms,

R⁷ represents hydrogen or

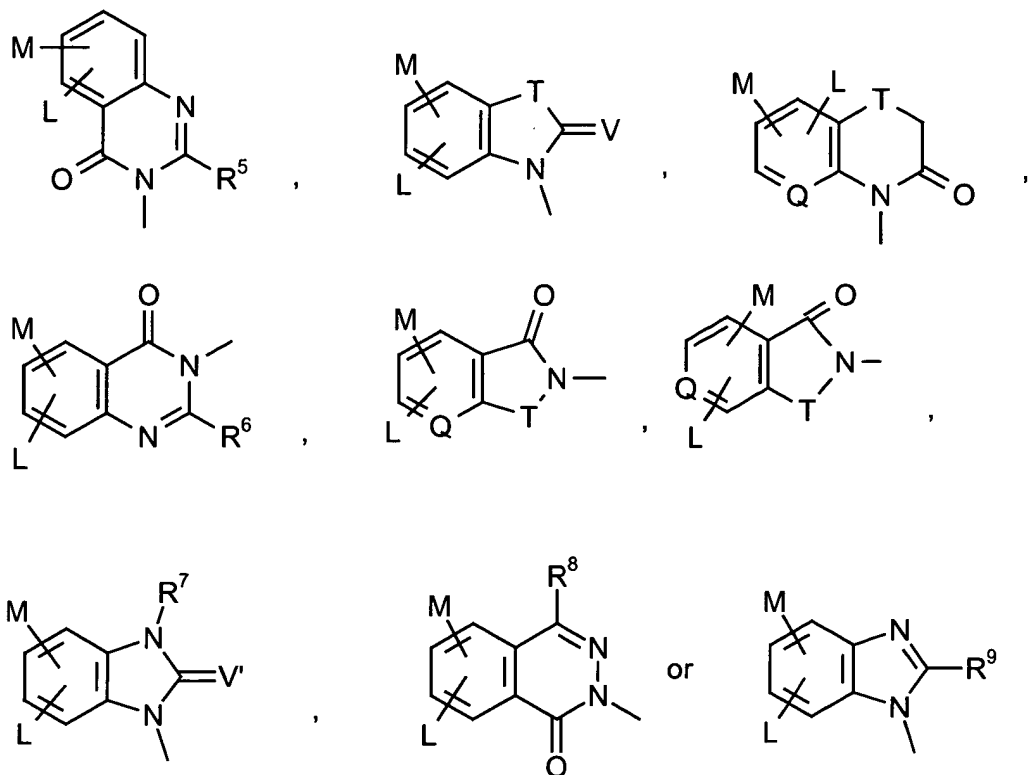
R⁶ and R⁷ together represent the group of the formula =O,

or of the general formula (A2)



in which

A represents a radical of the formula



in which

L and M are identical or different and

denote hydrogen, halogen, trifluoromethyl, carboxyl, cycloalkyl having 3 to 6 carbon atoms, hydroxyl, phenyl or straight-chain or branched alkyl, alkoxycarbonyl or alkoxy each having up to 6 carbon atoms,

Q denotes a nitrogen atom or the -CH- group,

T denotes a group of the formula -SO₂ or -CO or an oxygen or sulphur atom,

V denotes an oxygen or sulphur atom,

R⁵, R⁶, R⁷ and R⁸ are identical or different and
denote hydrogen, or straight-chain or branched alkyl having up to 6 carbon atoms, benzyl or phenyl, each of which is optionally substituted by halogen or by straight-chain or branched alkyl having up to 6 carbon atoms,

R⁹ denotes trifluoromethyl, benzyl or a 5- to 7-membered, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, which is optionally substituted up to 3 times, identically or differently, by halogen, phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms, or
denotes a group of the formula -S(O)_a-R¹⁰,

in which

a denotes a number 0, 1 or 2,

R¹⁰ denotes straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by straight-chain or branched acyl having up to 6 carbon atoms or by aryl or aroyl each having up to 10 carbon atoms, which for their part can be substituted up to 2 times, identically or differently, by halogen, trifluoromethyl or by straight-chain or branched acyl having up to 5 carbon atoms, or
denotes aryl having 6 to 10 carbon atoms, which is optionally substituted by halogen, hydroxyl, trifluoromethyl or straight-chain

or branched alkyl or alkoxy each having up to 5 carbon atoms,

D and E are identical or different and

represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

Z represents an oxygen or sulphur atom,

R¹ represents cycloalkyl having 3 to 10 carbon atoms or straight-chain or branched alkyl having 1 to 10 carbon atoms, or represents phenyl which is optionally substituted up to 2 times, identically or differently, by halogen, nitro, cyano, hydroxyl, straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

R² represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

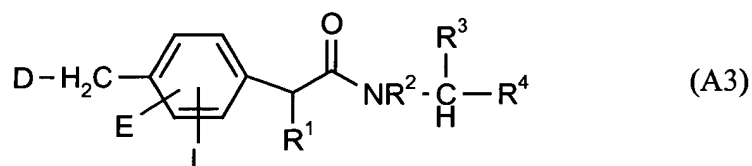
R³ represents hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms, or represents cycloalkyl having 3 to 7 carbon atoms, or represents phenyl or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, nitro, phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy having up to 6 carbon atoms,

R⁴ represents hydrogen or a group of the formula -CH₂-OH or CH₂O-CO-R¹¹,

in which

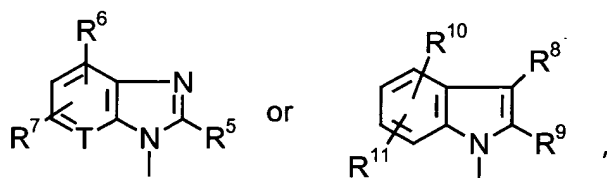
R^{11} denotes hydrogen, straight-chain or branched alkyl having up to 8 carbon atoms or phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl, cyano or straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

or of the general formula (A3)



in which

D represents a radical of the formula



in which

T denotes a nitrogen atom or the -CH- group,

R^6 , R^7 , R^{10} and R^{11} are identical or different and denote hydrogen, trifluoromethyl, halogen or straight-chain or branched

alkyl or alkoxy each having up to 6 carbon atoms,

R⁵, R⁸ and R⁹ are identical or different and

denote hydrogen, cycloalkyl having 3 to 6 carbon atoms, phenyl, straight-chain or branched alkoxy carbonyl having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by halogen,

or, if T represents a nitrogen atom, R⁵ can also denote benzyl,

E and L are identical or different and

represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxy carbonyl each having up to 6 carbon atoms,

R¹ represents cycloalkyl having 3 to 10 carbon atoms or straight-chain or branched alkyl having 1 to 10 carbon atoms, or represents phenyl which is optionally substituted up to 2 times, identically or differently, by halogen, cyano, hydroxyl, straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

R² represents hydrogen or straight-chain or branched alkyl having up to 3 carbon atoms,

R³ represents hydrogen or straight-chain or branched alkyl having up to 5 carbon atoms, or represents cycloalkyl having 3 to 7 carbon atoms, or represents phenyl or a 5- to 7-membered aromatic heterocycle having up to

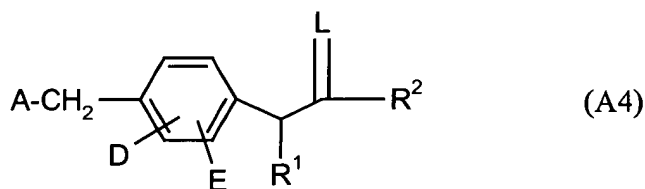
3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, nitro, phenyl, hydroxyl or by straight-chain or branched alkyl or alkoxy having up to 6 carbon atoms,

R⁴ represents hydrogen or a group of the formula -CH₂-OH or CH₂O-CO-R¹²,

in which

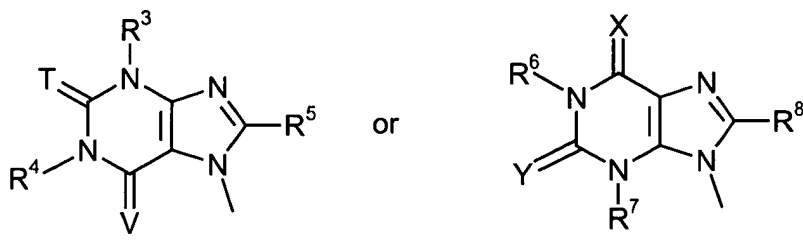
R¹² denotes hydrogen, straight-chain or branched alkyl having up to 8 carbon atoms or phenyl which is optionally substituted up to 3 times, identically or differently, by halogen, hydroxyl, cyano or straight-chain or branched alkyl or alkoxy each having up to 4 carbon atoms,

or of the general formula (A4)



in which

A represents a radical of the formula



in which

R^3 , R^4 , R^6 and R^7 are identical or different and

denote hydrogen, cycloalkyl having 3 to 7 carbon atoms or aryl having 6 to 10 carbon atoms,

or denote straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by halogen, hydroxyl or aryl having 6 to 10 carbon atoms,

T , V , X and Y are identical or different and denote an oxygen or sulphur atom,

R^5 and R^8 are identical or different and

denote hydrogen, halogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by cycloalkyl having 3 to 8 carbon atoms, or by a 5- to 6-membered, aromatic, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or by aryl having 6 to 10 carbon atoms, where the cyclic systems for their part can be substituted up to 3 times, identically or differently, by a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or by phenyl, benzyl, halogen, hydroxyl, carboxyl or by straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms, or

denote aryl having 6 to 10 carbon atoms or a 5- to 7-membered aromatic, optionally benzo-fused heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, each of which is optionally substituted up to 3 times, identically or differently, by halogen, phenyl, trifluoromethyl, hydroxyl, carboxyl or by straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or by a group of the formula $-(CO)_a-NR^9R^{10}$,

in which

a denotes a number 0 or 1,

R^9 and R^{10} are identical or different and

denote hydrogen, phenyl or straight-chain or branched alkyl or acyl each having up to 5 carbon atoms,

D and E are identical or different and

represent hydrogen, halogen, trifluoromethyl, hydroxyl, carboxyl or straight-chain or branched alkyl, alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

R^1 represents hydrogen or cycloalkyl having 3 to 8 carbon atoms, or represents straight-chain or branched alkyl or alkenyl each having up to 8 carbon atoms, each of which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms, phenyl or by a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, or represents phenyl or a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O, the ring systems optionally being substituted up to 3 times, identically or differently, by halogen,



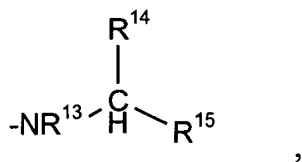
phenyl, trifluoromethyl or straight-chain or branched alkyl or alkoxy each having up to 5 carbon atoms, hydroxyl or by a group of the formula $-NR^{11}R^{12}$,

in which

R^{11} and R^{12} have the meaning of R^9 and R^{10} indicated above and are identical to or different from this,

L represents an oxygen or sulphur atom,

R^2 represents mercapto, hydroxyl, straight-chain or branched alkoxy having up to 8 carbon atoms or the group of the formula



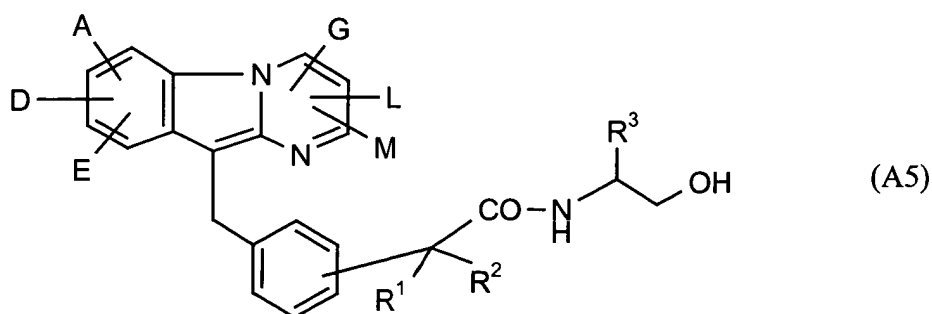
in which

R^{13} denotes hydrogen or straight-chain or branched alkyl having up to 4 carbon atoms,

R^{14} denotes hydrogen, phenyl or a 5- to 6-membered aromatic heterocycle having up to 3 heteroatoms from the group consisting of S, N and/or O,

R^{15} denotes hydrogen or straight-chain or branched alkyl having up to 8 carbon atoms, which is optionally substituted by hydroxyl,

or of the general formula (A5)



in which

A, D, E, G, L and M are identical or different and

represent hydrogen, halogen, trifluoromethyl, carboxyl, hydroxyl, straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

R¹ and R² are identical or different and

represent hydrogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl having up to 10 carbon atoms, which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms or

represent phenyl which is optionally substituted by halogen or trifluoromethyl, or

R¹ and R², together with the carbon atom, form a 4- to 8-membered cycloalkyl ring

and

R³ represents phenyl which is optionally substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,
and/or is optionally substituted by a group of the formula -OR⁴ or -NR⁵R⁶,

in which

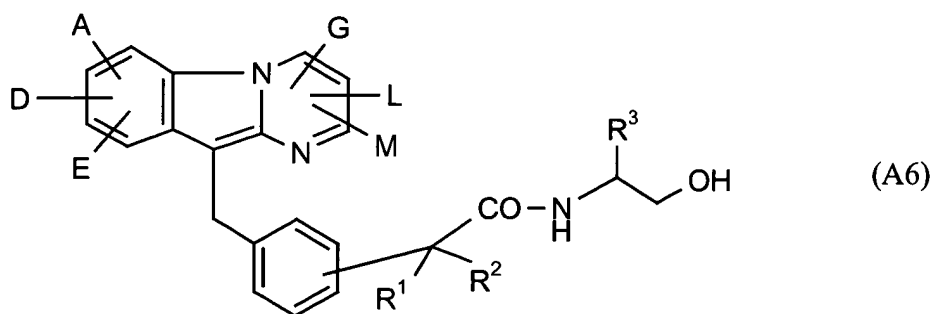
R⁴ denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

R⁵ and R⁶ are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
or denote straight-chain or branched acyl having up to 8 carbon atoms,
which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and
denote hydrogen or straight-chain or branched acyl having up to
8 carbon atoms,

or of the general formula (A6)



in which

A, D, E, G, L and M are identical or different and

represent hydrogen, halogen, trifluoromethyl, carboxyl, hydroxyl, straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms or straight-chain or branched alkyl having up to 6 carbon atoms, which for its part can be substituted by hydroxyl or by straight-chain or branched alkoxy having up to 4 carbon atoms,

R¹ and R² are identical or different and

represent hydrogen, cycloalkyl having 3 to 8 carbon atoms or straight-chain or branched alkyl having up to 10 carbon atoms, which is optionally substituted by cycloalkyl having 3 to 6 carbon atoms, or

represent phenyl which is optionally substituted by halogen or trifluoromethyl, or

R¹ and R², together with the carbon atom, form a 4- to 8-membered cycloalkyl ring

and

R³ represents phenyl which is optionally substituted up to 3 times, identically or differently, by nitro, carboxyl, halogen, cyano or by straight-chain or branched alkenyl or alkoxycarbonyl each having up to 6 carbon atoms or by straight-chain

or branched alkyl having up to 6 carbon atoms, which is optionally substituted by hydroxyl, carboxyl or by straight-chain or branched alkoxy or alkoxycarbonyl each having up to 6 carbon atoms,

and/or is optionally substituted by a group of the formula $-OR^4$ or $-NR^5R^6$,

in which

R^4 denotes hydrogen or straight-chain or branched alkyl or alkenyl each having up to 6 carbon atoms,

R^5 and R^6 are identical or different and denote phenyl, hydrogen or straight-chain or branched alkyl having up to 6 carbon atoms,
or denote straight-chain or branched acyl having up to 8 carbon atoms,
which is optionally substituted by a group of the formula $-NR^7R^8$,

in which

R^7 and R^8 are identical or different and
denote hydrogen or straight-chain or branched acyl having up to
8 carbon atoms,

if appropriate in an isomeric form and their salts

and component B being at least one [with] HMG-CoA reductase inhibitor[s] [as component B for the production of medicaments for the prophylaxis and/or treatment of cardiovascular diseases].



2. (Amended) [Use of a combination] The method according to Claim 1 [for the production of medicaments for the control or prophylaxis of] wherein said cardiovascular diseases [which] are associated with metabolic diseases or deficits.
3. (Amended) [Use of a combination] The method according to Claim 2 for the control of arteriosclerosis, diseases of the coronary vessels of the heart, raised serum lipids, hypercholesterolaemia, hypertriglyceridaemia and mixed forms which are combined with raised VLDL or LDL and/or raised chylomicrons, and of syndrome X.
4. (Amended) [Use of a combination] The method according to Claim 2 for the treatment of secondary hypercholesterolaemia and secondary hypertriglyceridaemia, which are optionally associated with apolipoprotein E polymorphism, obesity, chylomicronaemia and chylomicronaemia syndrome, renal insufficiency, chronic renal insufficiency, nephrotic syndrome, diabetes mellitus type II, and with hepatomas and plasmacytomas.
5. (Amended) [Use of a combination] The method according to Claim 2, characterized in that [it contains, as] component A[,] is a compound of the general formula (A1).
6. (Amended) [Use of a combination] The method according to Claim 2, characterized in that [it contains, as] component A[,] is a compound of Examples 1-119.
7. (Amended) [Use of a combination] The method according to Claim 2, characterized in that [it contains, as] component A[,] is a compound of Examples 92-119.
8. (Amended) [Use of a combination] The method according to Claim 2, characterized in that [it contains, as] component A[,] is a compound of Examples 48 or 80.

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9. (Amended) [Medicament] A pharmaceutical composition comprising a combination of an MTP inhibitor as component A and an HMG-CoA reductase inhibitor as component B according to Claim 1 and, if appropriate, one or more further suitable components.
10. (Amended) [Medicament] A pharmaceutical composition according to Claim 9, characterized in that it contains, as component A, the active compound 2-cyclopentyl-2-[4-(2,4-dimethyl-pyrido[2,3-b]indol-9-ylmethyl)-phenyl]-N-(2-hydroxy-1-phenyl-ethyl)-acetamide or 2-cyclopentyl-2-[4-(2,4-dimethyl-pyrimido[1,2-a]indol-10-ylmethyl)-phenyl]-N-(2-hydroxy-1-phenyl-ethyl)-acetamide and, as component B, the active compound atorvastatin, cerivastatin, simvastatin, pravastatin, lovastatin, fluvastatin, itavastatin or ZD 4522.
11. (Amended) [Medicament] A pharmaceutical composition according to Claim 9, characterized in that it contains, as component A, the compound (2S)-2-cyclopentyl-2-[4-(2,4-dimethyl-pyrido[2,3-b]indol-9-ylmethyl)-phenyl]-N-(2-(1R)-hydroxy-1-phenyl-ethyl)-acetamide.
12. (Amended) [Process] A process for the production of [medicaments] a pharmaceutical composition according to Claim 9, characterized in that the components A and B are converted into a suitable administration form with excipients and vehicles and, if appropriate, with further components.